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EXAMINER	
RAGHU, GANAPATHIRAM	
ART UNIT	PAPER NUMBER
1652	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,841	TANIGUCHI ET AL.	
	Examiner	Art Unit	
	GANAPATHIRAMA RAGHU	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,7,23-27,29 and 30* is/are pending in the application.

4a) Of the above claim(s) *23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,7 and 24-27, 29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Application Status

Please note that the instant application/case has been transferred to examiner Ganapathirama Raghu, Art Unit 1652, whose telephone number is (571)-272-4533 and all further enquiries regarding this application should be directed to said examiner.

In response to the Non-Final Office Action dated 07/11/08, applicants' response with claim amendments on 12/11/08 is acknowledged. Said response amended claims 7, 23, 24 and 30. Claims 6, 7, 23-27, 29 and 30 are currently pending in this application Applicants' request to rejoin claim 23 is noted, however upon further review, none of the claims are in condition for allowance and therefore claim 23 drawn to a method remains withdrawn as said claim is directed to non-elected invention. Thus claims 6, 7, 24-27, 29 and 30 are under consideration in the instant Office Action.

Objections and rejections not reiterated from previous action are hereby withdrawn.

Withdrawn-Claim rejections: 35 USC § 112, second paragraph,

Previous rejection of claims 7, 24 and 30 rejected under 35 USC § 112, second paragraph, is being withdrawn due to claim amendments and persuasive arguments by the applicants.

Withdrawn-Claim rejections: 35 USC § 112, first paragraph,

Previous rejection of claims 7, 24 and 30 rejected under 35 USC § 112, first paragraph, is being withdrawn due to claim amendments and persuasive arguments by the applicants.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). This application is a 371 of PCT/JP02/13879 filed on 12/27/2002 and claims the priority date of Japanese application 2002-2056 filed on 01/09/2002. Examiner notes that the certified copy of the Japanese application 2002-205 is provided on 07/07/2004. However, English translation for the said Japanese application is not provided and hence for examination purposes the effective date for the instant claims are the filing date of 371 of PCT/JP02/13879 filed on 12/27/2002.

New-Claim Rejections: 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 25 (claims 24, 26, 27, 29, 30, 6 and 7 depending therefrom) are rejected under 35 U.S.C. 101, because the claim reads on non-statutory subject matter. Claims 25 is drawn to 'A polypeptide fragment…', which reads on the product of nature. Claims directed to such subject matter are considered non-statutory because they read on products of nature. Examiner suggests amending the claim to recite 'An isolated polypeptide fragment …', to show the hand of man, in order to overcome the rejection.

New-Claim Rejections: 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claim 25 and claims 6, 7, 24, 26, 27 depending therefrom are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an

isolated polypeptide fragment consisting of the amino acid sequence of SEQ ID NO: 7 and having neovasularization activity and pharmaceutical compositions comprising said polypeptide sequence, does not reasonably provide enablement for: i) any polypeptide fragment of any N-acetylglucosaminyltransferase (GnT-V) of undefined structure from any source including variants, mutants and recombinants, said polypeptide comprising any basic amino acid cluster region having neovasularization activity or ii) comprising (open language) the amino acid sequence of SEQ ID NO: 7 and any 50 contiguous amino acids encoded by the SEQ ID NO: 6 at either amino or carboxy termini of SEQ ID NO: 7 or any variant thereof and having neovasularization activity (as in claims 25-27) and pharmaceutical compositions comprising said polypeptides (as in claims 6, 7 and 24). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with the claim.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claim 25 and claims 6, 7, 24, 26, 27 depending therefrom are so broad as to encompass: i) any polypeptide fragment of any N-acetylglucosaminyltransferase (GnT-

V) of undefined structure from any source including variants, mutants and recombinants, said polypeptide comprising any basic amino acid cluster region having neovasularization activity or ii) comprising (open language) the amino acid sequence of SEQ ID NO: 7 and any 50 contiguous amino acids encoded by the SEQ ID NO: 6 at either amino or carboxy termini of SEQ ID NO: 7 or any variant thereof and having neovasularization activity (as in claims 25-27) and pharmaceutical compositions comprising said polypeptides (as in claims 6, 7 and 24). The scope of the claims are not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides having neovascularization activity and encoding polynucleotides broadly encompassed by the claim. Since the amino acid sequence of a protein encoded by a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires knowledge and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. In view of the broad breadth of the claim, the amount of experimentation required to determine the structure of all the polypeptides or encoding polynucleotides from any source as recited in the claims, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Whisstock et al., Q Rev Biophys. 2003 Aug; 36(3): 307-

340), practicing the claimed invention would require undue experimentation. As such, the specification fails to enable the entire scope of the claimed invention.

However, in this case the disclosure is limited to an isolated polypeptide fragment consisting of the amino acid sequence of SEQ ID NO: 7 and having neovasularization activity and pharmaceutical compositions comprising said polypeptide sequence, but provides no guidance with regard to the making and using of variants and mutants i.e., i) any polypeptide fragment of any N-acetylglucosaminyltransferase (GnT-V) of undefined structure from any source including variants, mutants and recombinants, said polypeptide comprising any basic amino acid cluster region having neovasularization activity or ii) comprising (open language) the amino acid sequence of SEQ ID NO: 7 and any 50 contiguous amino acids encoded by the SEQ ID NO: 6 at either amino or carboxy termini of SEQ ID NO: 7 or any variant thereof and having neovasularization activity (as in claims 25-27) and pharmaceutical compositions comprising said polypeptides (as in claims 6, 7 and 24). In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Whisstock et al., Q Rev Biophys. 2003 Aug; 36(3): 307-340), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides and encoding polynucleotides encompassed by the claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is not routine in the art to screen for multiple substitutions or multiple

modifications as encompassed by the instant claim, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions or deletions.

The specification does not support the broad scope of the claim which encompasses: i) any polypeptide fragment of any N-acetylglucosaminyltransferase (GnT-V) of undefined structure from any source including variants, mutants and recombinants, said polypeptide comprising any basic amino acid cluster region having neovasularization activity or ii) comprising (open language) the amino acid sequence of SEQ ID NO: 7 and any 50 contiguous amino acids encoded by the SEQ ID NO: 6 at either amino or carboxy termini of SEQ ID NO: 7 or any variant thereof and having neovasularization activity (as in claims 25-27) and pharmaceutical compositions comprising said polypeptides (as in claims 6, 7 and 24), because the specification does not establish: (A) regions of the protein/polynucleotide structure which may be modified without affecting the activity of the encoded polypeptide having neovasularization activity; (B) the general tolerance of the polypeptide and the polynucleotide encoding neovasularization activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue or the respective codon in the polynucleotide with an expectation of obtaining the desired biological function; and (D)

the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claim broadly including polypeptides and encoding polynucleotides with an enormous number of modifications. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides and encoding polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claim 25 and claims 6, 7, 24, 26, 27 depending therefrom are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 25 and claims 6, 7, 24, 26, 27 depending therefrom as interpreted are directed to encompass: i) <u>any</u> polypeptide fragment of any N-acetylglucosaminyltransferase (GnT-V) of undefined structure from any source including variants, mutants and recombinants, said polypeptide comprising any basic amino acid

cluster region having neovasularization activity or ii) comprising (open language) the amino acid sequence of SEQ ID NO: 7 and any 50 contiguous amino acids encoded by the SEQ ID NO: 6 at either amino or carboxy termini of SEQ ID NO: 7 or any variant thereof and having neovasularization activity (as in claims 25-27) and pharmaceutical compositions comprising said polypeptides (as in claims 6, 7 and 24).

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case the scope of the instant claims encompass a genus of structures (no structural limitation), polypeptides of interest and encoding polynucleotides i.e., i) any polypeptide fragment of any N-acetylglucosaminyltransferase (GnT-V) of undefined structure from any source including variants, mutants and recombinants, said polypeptide comprising any basic amino acid cluster region having neovasularization activity or ii) comprising (open language) the amino acid sequence of SEQ ID NO: 7 and any 50 contiguous amino acids encoded by the SEQ ID NO: 6 at either amino or carboxy termini of SEQ ID NO: 7 or any variant thereof and having

neovasularization activity (as in claims 25-27) and pharmaceutical compositions comprising said polypeptides (as in claims 6, 7 and 24).

No information, beyond the characterization of an isolated polypeptide fragment consisting of the amino acid sequence of SEQ ID NO: 7 and having neovasularization activity and pharmaceutical compositions comprising said polypeptide sequence has been provided by the applicants, which would indicate that they had possession of the claimed encompass a genus of structures (no structural limitation), polypeptides of interest and encoding polynucleotides i.e., i) any polypeptide fragment of any N-acetylglucosaminyltransferase (GnT-V) of undefined structure from any source including variants, mutants and recombinants, said polypeptide comprising any basic amino acid cluster region having neovasularization activity or ii) comprising (open language) the amino acid sequence of SEQ ID NO: 7 and any 50 contiguous amino acids encoded by the SEQ ID NO: 6 at either amino or carboxy termini of SEQ ID NO: 7 or any variant thereof and having neovasularization activity (as in claims 25-27) and pharmaceutical compositions comprising said polypeptides (as in claims 6, 7 and 24).

The art also teaches, even highly structurally homologous polypeptides do not necessarily share the same function and conversely functionally similar molecules do not necessarily have similar structures. For example proteins having similar structure have different activities; Witkowski et al., (Biochemistry 38:11643-11650, 1999) teaches that one conservative amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Similarly, Wishart et al., (J. Biol. Chem., 1995, Vol. 270(10): 26782-26785) teach that a

single mutation converts a novel phosphotyrosine binding domain into a dual-specificity phosphatase. The art also teaches that functionally similar molecules have different structures; Kisselev L., (Structure, 2002, Vol. 10: 8-9) teach that polypeptide release factors in prokaryotes and eukaryotes have same function but different structures.

Hence, the recited genera of polypeptides and encoding polynucleotides as claimed are interpreted to have widely variable structures, since minor changes may result in changes affecting function and no additional information correlating structure with function has been provided.

Therefore, given the lack of description of representative species encompassed by the genus of polypeptides and encoding polynucleotides and modifications, the specification fails to sufficiently describe the claimed invention in full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention. Applicants are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

New-Claim Rejections 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6, 7, 24-27, 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Taniguchi et al., (Glycoconjugate Journal, 2001 (November), Vol. 18 (11-

12): 859-865, in IDS). Claims 6, 7, 24-27, 29 and 30 are directed to: i) any polypeptide fragment of any N-acetylglucosaminyltransferase (GnT-V) of undefined structure from any source including variants, mutants and recombinants, said polypeptide comprising any basic amino acid cluster region having neovasularization activity or ii) comprising (open language) the amino acid sequence of SEQ ID NO: 7 and any 50 contiguous amino acids encoded by the SEQ ID NO: 6 at either amino or carboxy termini of SEQ ID NO: 7 or any variant thereof and having neovasularization activity (as in claims 25-27) and pharmaceutical compositions comprising said polypeptides (as in claims 6, 7 and 24).

Taniguchi et al., (*supra)* disclose the basic amino acid cluster corresponding to amino acid residues 254-269 having the peptide sequence KSVRGKGQKRKRKK, same as SEQ ID NO: 7 of the instant invention comprised in the polypeptide encoded by the polynucleotide of SEQ ID NO: 6 and having angiogenic or neovasularization activity (page 863, column 1, paragraph 2; and page 864, column 1, paragraph 2). Said reference also discloses that said polypeptide having diagnostic and therapeutic potential i.e., pharmaceutical composition (page 863, column 2, Discussion section, paragraph 3; and Future perspectives, column 2, page 864). Therefore, the reference of Taniguchi et al., (Glycoconjugate Journal, 2001 (November), Vol. 18 (11-12): 859-865, in IDS) anticipates claims 6, 7, 24-27, 29 and 30 as written.

Summary of Pending Issues

The following is a summary of issues pending in the instant application.

1. Claim 25 (claims 24, 26, 27, 29, 30, 6 and 7 depending therefrom) are rejected

under 35 U.S.C. 101, because the claim reads on non-statutory subject matter.

2. Claim 25 and claims 6, 7, 24, 26, 27 depending therefrom are rejected under 35 U.S.C. 112, first paragraph for enablement and written description.

3. Claims 6, 7, 24-27, 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Taniguchi et al., (Glycoconjugate Journal, 2001 (November), Vol. 18 (11-12): 859-865, in IDS).

Conclusion

None of the claims are allowable. Claims are rejected for the reasons identified in the Rejections and Summary sections of this Office Action. Applicants must respond to the objections/rejections in each of the sections in this Office Action to be fully responsive for prosecution.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ganapathirama Raghu/
Patent Examiner
Art Unit 1652